Claim 2 (Amended) The isolated polynucleotide according to claim 1, [being] wherein said isolated polynucleotide is at least 50% homologous, preferably more than 70% homologous, more [preferred] preferably more than 80% homologous, even more [preferred] preferably more than 90% homologous, and most [preferred] preferably more than 95%[,] homologous to the polynucleotide sequence [presented as] of SEQ ID NO: 1.

Claim 3 (Amended) The isolated polynucletoide according to [either of claims 1-2 being] claim 1, wherein said isolated polynucleotide is a cloned polynucleotide.

Claim 4 (Amended) The isolated polynucletoide according to claim 3, [in which] wherein the polynucleotide is cloned from, or produced [on the basis of] from a cDNA library.

Claim 5 (Amended)

Line 1, change "any of claims 1-4" to --claim 1--

Line 2, change "presented as" to --of--

Line 3, change "hereof" to --thereof--

Claim 6 (Amended) The isolated polynucletoide according to [any of claims 1-4] claim 1, comprising the polynucleotide sequence [presented as] of SEQ ID NO: 1, or a sub-sequence [hereof, including the] thereof, wherein said sequence includes a mutation G935A.

Claim 7 (Amended) The isolated polynucletoide according to [any of claim 1-6, encoding] claim 1, wherein said isolated polynucleotide encodes a potassium channel, or a potassium channel subunit.

Claim 8 (Amended)

Line 1, change "the" (second occurrence) to --a--

Line 2, change "represented by" to --of--

Line 3, change "hereof" to --thereof--

Claim 9 (Amended)

Line 2, change "which" to --wherein said--

Claim 10 (Amended) The isolated polynucletoide according to claim 9, [which] wherein said variant has an amino acid sequence that has been changed at one or more positions located in [the] a conserved [regions, as] region, wherein said region is defined by Table 1.

Claim 11 (Amended) The isolated polynucletoide according to claim 9, encoding [the] a variant KCNQ4/G285S [(i.e. KCNQ4/G333S according to the KCNQ1 numbering)] or KCNQ4/G333S when said polynucleotide is numbered according to KCNQ1.

Claim 12 (Amended)

Line 1, change "set forth in" to --of--

Claim 13 (Amended)

Line 2, change "claims 1-11" to --claim 1--

Claim 14 (Amended) The polypeptide according to claim 13, [being] wherein said polypeptide is a KCNQ4 potassium channel subunit comprising the amino acid sequence [presented as] of SEQ ID No. 2.

Claim 15 (Amended) The polypeptide according to claim 13, [being a] wherein said polypeptide is a KCNQ4 variant, [which] and wherein said variant has an amino acid sequence that has been changed by deletion of an amino acid residue, by insertion of an additional amino acid residue, or by substitution of an amino acid residue at one or more positions.

Claim 16 (Amended) The polypeptide according to claim 15, [which] wherein said variant has an amino acid sequence that has been changed at one or more positions located in [the] a conserved [regions, as] region, wherein said region is defined by Table 1.

Claim 17 (Amended) The polypeptide according to claim 15, [being] wherein said polypeptide is the variant KCNQ4/G285S [(i.e. KCNQ4/G333S according to the KCNQ1 numbering)] or KCNQ4/G333S when said polypeptide is numbered according to KCNQ1.

Claim 18 (Amended)

Line 2, change "any of claims 1-11" to --claim 1--

Claim 19 (Amended)

Line 2, change "presented as" to --of--

Line 3, change "hereof" to --thereof--

Claim 20 (Amended)

Line 2, change "which" to --wherein said--

Claim 21 (Amended) The cell according to claim 20, [which] wherein said variant has an amino acid sequence that has been changed at one or more positions located in [the] a conserved [regions, as] region, wherein said region is defined by Table 1.

Claim 22 (Amended) The cell according to claim 20, genetically manipulated by the incorporation of the variant KCNQ4/G285S [(i.e. KCNQ4/G333S according to the KCNQ1 numbering)] or KCNQ4/G333S when numbered according to KCNQ1.

Claim 23 (Amended) The cell according to [any of claims 18-22, genetically manipulated to co-express] claim 18, wherein said cell co-expresses one or more KCNQ channel subunits.

Claim 24 (Amended) The cell according to 23, [genetically manipulated to co-express] wherein said cell co-expresses KCNQ4 and KCNQ1 channel subunits[;], KCNQ4 and KCNQ2 channel subunits[;], KCNQ4 and KCNQ3 channel subunits[;], KCNQ4 and KCNQ1 and KCNQ2 channel subunits[;], KCNQ4 and KCNQ1 and KCNQ3 channel

subunits[;], KCNQ4 and KCNQ2 and KCNQ3 channel subunits[;], or KCNQ4 and KCNQ1 and KCNQ2 and KCNQ3 channel subunits.

Claim 25 (Amended) The cell according to claim 23, [genetically manipulated to co-express] wherein said cell co-expresses KCNQ3 and KCNQ4 channel subunits.

Claim 26 (Amended) The cell according to [any of claims 18-25, being] claim 18, wherein said cell is an eukaryotic cell, in particular a mammalian cell, an oocyte, or a yeast cell.

Claim 27 (Amended) The cell according to [any] claim 26, [being] wherein said cell is a human embryonic kidney (HEK) cell, a HEK 293 cell, a BHK21 cell, a Chinese hamster ovary (CHO) cell, a *Xenopus laevis* oocyte (XLO) cell, a COS cell, or any other cell line [able to express] that expresses KCNQ potassium channels.

Claim 28 (Amended)

Line 1, change "any of claims 18-27" to --claim 18--

Claim 29 (Amended) A method for obtaining a substantially homogeneous source of a human potassium channel[,] comprising a KCNQ4 subunit, [which method comprises] comprising the steps of:

culturing a cellular host having incorporated expressibly therein a polynucleotide according to [any of claims 1-11, and then] claim 1; and

recovering the cultured cells.

Claim 30 (Amended)

Line 1, before "comprising" insert --further-- and delete "subsequent"

Claim 31 (Amended) A method of [screening] detecting a chemical compound [for capability of binding] which binds to a potassium channel comprising at least one KCNQ4 channel subunit[, which method comprises] comprising the steps of:

(i) subjecting a KCNQ4 channel subunit [containing] of a cell [according to claims 18-27,] or a membrane preparation [according to claim 28,] to the action of a KCNQ4 binding agent to form a complex [with the KCNQ4 channel subunit containing cell];

(ii) subjecting the complex of step (i) to the action of the chemical compound to be tested; and

(iii) detecting the displacement of the KCNQ4 binding agent from the complex with the KCNQ4 channel subunit [containing] of the cell or membrane preparation.

Claim 32 (Amended) The method of claim 31, wherein the cell containing the KCNQ4 channel subunit [containing cell] is a cell [according to any of claims 18-27, or a membrane preparation according to claim 28] which is genetically manipulated by the incorporation of a heterologous polynucleotide having a nucleic acid sequence which is capable of hybridizing under high

stringency conditions with the polynucleotide of SEQ ID NO. 1, its complimentary strand, or a sub-sequence thereof.

Claim 33 (Amended)

Line 1, change "either of claims 31-32, in which" to --claim 31, wherein--

Line 3, change "(Linopirdine);" to --(Linopirdine),--

Claim 34 (Amended) The method of claim 33, [which compounds have been marked] wherein said binding agents are radioactively labelled with ^{3}H.

Claim 35 (Amended)

Line 1, change "either of claims 33-34" to --claim 33--

Line 2, delete "containing"

Line 3, change "the" to --an--

Claim 36 (Amended) A method of screening a chemical compound for activity on a potassium channel comprising at least one KCNQ4 channel subunit, [which method comprises] comprising the steps of:

(i) subjecting a KCNQ4 channel subunit [containing] of a cell to the action of the chemical compound; and

(ii) monitoring the membrane potential, the current, the potassium flux, or the secondary calcium influx of the KCNQ4 channel subunit [containing] of said cell.

Claim 37 (Amended)

Line 1, change "the KCNQ4 channel subunit containing" to --said--

Line 2, change "any of claims 18-27" to --claim 18--

Claim 38 (Amended)

Line 1, change "either of claims 36-37" to --claim 36--

Line 2, delete "of the KCNQ4 channel subunit containing cell"

Claim 39 (Amended)

Line 1, change "either of claims 36-37" to --claim 36--

Line 2, delete "of the KCNQ4 channel subunit containing cell" and change "using" to --by--

Claim 40 (Amended)

Line 1, change "claims 31-35, and/or by the" to --claim 31--

Line 2, delete "method of claims 36-39"

Claim 41 (Amended) [Use of the chemical compound according to claim 40 for] A method of diagnosis, treatment, prevention or alleviation of diseases related to tinnitus, loss of hearing, [in particular] progressive hearing loss, neonatal deafness, and presbyacusis, [(deafness of the elderly); and] diseases of adverse conditions of the CNS, [including] affective disorders, Alzheimer's disease, anxiety, ataxia, CNS damage caused by trauma, stroke or neurodegenerative illness, cognitive deficits,

compulsive [behaviour] behavior, dementia, depression, Huntington's disease, mania, memory impairment, memory disorders, memory dysfunction, motion disorders, motor disorders, neurodegenerative diseases, Parkinson's disease and Parkinson-like motor disorders, phobias, Pick's disease, psychosis, schizophrenia, spinal cord damage, stroke, and tremor comprising the step of:

using a chemical compound of claim 40.

Claim 42 (Amended)

Line 1, change "use" to --method--

Line 2, change "(Linopirdine);" to --(Linopirdine),--

Claim 43 (Amended) [Use of a polynucleotide sequence according to any of claims 1-12, for the] A method for screening [of] genetic materials [for] of individuals [having this mutations] comprising:

contacting a polynucleotide of claim 1 to said genetic material; and

detecting hydridization of said polynucleotide to said genetic material.

Claim 44 (Amended)

Line 2, change "gene, a" to --gene or a-- and change "gene, or genetically manipulated in order to over-" to --gene.--

Line 3, delete in its entirety.

Claim 45 (Amended)

The transgenic animal according to claim 44, [being a knock-out animal in which the gene is totally deleted] wherein said knock-out is in a homozygous state.

Claim 47 (Amended) The transgenic animal according to [any of claims 44-46, being] claim 44, wherein said transgenic animal is a transgenic rodent, in particular a hamster, a guinea pig, a rabbit, or a rat, a transgenic pig, a transgenic cattle, a transgenic sheep, or a transgenic goat.

Claim 49 (Amended) [The use according to claim 48, for the screening of] A method to screen for drugs affecting diseases or conditions associated with hearing loss or tinnitus, comprising injecting a transgenic animal of claim 44 with a therapeutic compound.

Claim 50 (Amended) A method for [the identification, localization, isolation or amplification] identifying, localizing, isolating or amplifying a polynucleotide [according to any one of claim 1-11], comprising using a polynucleotide according to claim 12 as a primer or a probe.

Claim 51 (Amended) An antibody capable of binding one or more polypeptides [as claimed in any one or claims 13-17] according to claim 13.

Claim 52 (Amended) The antibody of claim 51, [being a] wherein said antibody is a monoclonal antibody.

Please add the following new claims:

--53. The method of claim 31, wherein a membrane preparation is used.

54. A chemical compound identified by the method of claim 36.

55. A method of diagnosis, treatment, prevention or alleviation of diseases related to tinnitus, loss of hearing, progressive hearing loss, neonatal deafness, and presbyacusis, diseases of adverse conditions of the CNS, affective disorders, Alzheimer's disease, anxiety, ataxia, CNS damage caused by trauma, stroke or neurodegenerative illness, cognitive deficits, compulsive behavior, dementia, depression, Huntington's disease, mania, memory impairment, memory disorders, memory dysfunction, motion disorders, motor disorders, neurodegenerative diseases, Parkinson's disease and Parkinson-like motor disorders, phobias, Pick's disease, psychosis, schizophrenia, spinal cord damage, stroke, and tremor comprising the step of:

using a chemical compound of claim 54.

56. The method according to claim 55, wherein the chemical compound is 1,3-dihydro-1-phenyl-3,3-bis(4-pyridylmethyl)-2H-indol-2-one (Linopirdine), or 10-10-bis(4-pyridinyl-methyl)-9(10H)-antracenone.

57. A transgenic animal that overexpresses a KCNQ4 gene or a mutated KCNQ4 gene.

58. The transgenic animal according to claim 57, wherein said transgenic animal is a transgenic rodent, in particular a hamster, a guinea pig, a rabbit, or a rat, a transgenic pig, a transgenic cattle, a transgenic sheep, or a transgenic goat.--

REMARKS

Entry of the above amendments is earnestly solicited. An early and favorable first action on the merits is earnestly solicited.